FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 10/29/2009.

Claims 2-5, 10, 11, 15-18, 20-25, 28-32, and 34-37 have been cancelled.

Claims 1, 8, 12, 19, 26, and 33 have been amended and incorporate no new matter.

New claims 38-41 have been added.

Claims 8, 9, 13, 19, and 38 stand withdrawn as being drawn to nonelected species.

Thus, claims 1, 6, 7, 12, 14, 26, 27, 33, and 39-41 now represent all claims currently pending and under consideration.

ELECTION/RESTRICTION

Applicant maintains a traversal of the requirement for restriction and species election made in the Office Action dated 2/23/2009, on the grounds that the cited reference, Bellini et al., fails to disclose compounds falling within the scope of the presently amended claims (Remarks, p. 13). In response, it is noted that the restriction requirement was withdrawn, and the species election requirement was maintained and made final, in the Office Action dated 5/29/2009, such that Groups I and II have been rejoined. However, Applicant is also reminded that, where a requirement to restrict is made and thereafter withdrawn as improper, if restriction becomes proper at a later stage in the prosecution, restriction may again be required. See MPEP §811.03.

Further, Bellini et al. discloses compounds falling within the scope of the claims that were pending on 2/23/2009, such that unity of invention was absent at that time. The Examiner is unaware of a legal basis under which unity of invention can be restored

retroactively. As to the species election requirement, Applicant's attention is directed to page 6 of the Office Action dated 2/23/2009, which states that "upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141." See MPEP §803.02.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been submitted.

WITHDRAWN OBJECTIONS/REJECTIONS

Objections

Due to the amendments to the specification, the objection to the specification has been withdrawn.

Rejections under 35 USC §112

Due to amendments to the claims, the rejection of claim 33 under 35 USC 112, first paragraph, has been withdrawn.

Due to amendments to the claims, the rejection of claim 1 under 35 USC 112, second paragraph, has been withdrawn.

Rejections under 35 USC §103

Applicant's arguments, see Remarks, pp. 14-15, filed 10/29/2009, with respect to the rejection of claims 1, 2, 6, 7, 26, 27, 33, and 37 as obvious over Lee et al. and Mintz et al., have been fully considered and are persuasive. Therefore, this rejection has been withdrawn.

NEW OBJECTIONS/REJECTIONS

Claim Objections

1. Claims 1, 39, and 41 are objected to because of the following informalities:

- In claim 1, p, 4. line 1, "R1 represents a a moiety" should be amended to "R1 represents a moiety";
- In claim 1, p. 4, line 5, in the definition of R2, "p is an integer from 1 and 5" should be amended to "p is an integer from 1 to 5";
- In claim 1, p. 4, line 14, "at least one R is different from hydrogen" could be amended to "at least one R is not hydrogen";
- In claim 1, p. 7, both structural formulae XX and XXI should be lined through;
- In claims 39 and 41, "flouroquinolones" should be spelled "fluoroquinolones," and "hydrocortosone" should be spelled "hydrocortisone";
- In claim 41, "terapeutically" should be spelled "therapeutically."

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 26 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The scope of these claims is indefinite for the following reasons:

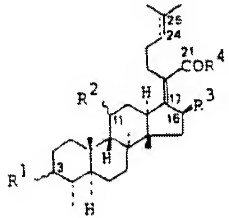
- **Claim 26** recites compounds which do not fall within the scope of claim 1, specifically the last four newly added compounds on page 11, which are branched polyamine groups only, with no steroid group. For clarity, the remaining recited species are interpreted to correspond to compounds 101, 102, 103, 105, 109, 110, 111, 112, 113, 115-121, and 123-125, as disclosed on specification pp. 22-29.

- **Claim 41** depends from claim 35; however, claim 35 has been cancelled. For examination purposes, claim 41 is interpreted as depending from claim 40.

Claim Rejections - 35 USC § 103

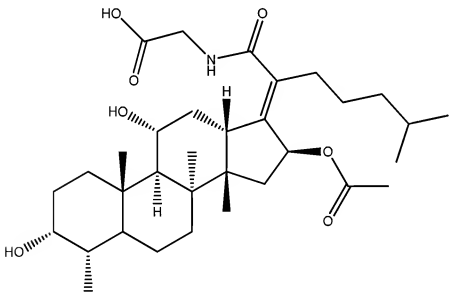
4. Claims 1, 6, 7, 12, 14, 26, 27, 33, and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bendtzen (WO90/04398) in view of Mintz et al. (USPN 5,744,453).

Bendtzen (p. 21) discloses compounds of general formula (A),



A

in particular compound XVIa, wherein the C_{24}-C_{25} bond is a single bond; R1 and R2 are α-OH; R3 is –O-C(O)-CH_3; and R4 is the sodium salt of –NH-CH2-C(O)OH, having the structural formula,



Bendtzen further discloses that "it is well-known that fusidic acid inhibits bacterial protein synthesis and it may be bacteriostatic and/or bactericidal. It is especially active against *Staphylococcus aureus*, including strains that are resistant to the penicillins or to

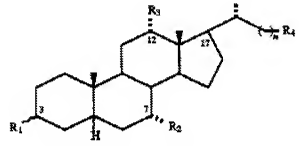
other antibiotics" (p. 2, line 17 to p. 3, line 2), and that derivatives of fusidic acid can be administered in methods of treating, *inter alia*, septic shock caused by gram-negative bacteria (abstract), as recited by claims 33, 40, and 41. Specifically, Bendtzen (p. 34, line 25 to p. 35, line 2) notes that the disclosed compounds are useful for

> prophylaxis or treatment of septic shock caused by gram-negative bacteria. Fusidic acid has been used for treatment of infections caused by gram-positive bacteria such as Staphylococcus aureus, but prior to the present invention it was not known that fusidic acid could be used for prophylaxis or treatment of septic shock which is caused by gram-negative bacteria. The present invention relates in particular to the use of fusidic acid or a derivative thereof for prophylaxis or treatment of septic shock caused by gram-negative bacteria for oral or parenteral administration.

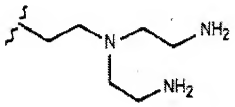
Thus, Bendtzen further teaches the disclosed compounds in pharmaceutical compositions (p. 24, line 25 to p. 28, line 28), as recited by claims 27 and 39, which can be administered in combination with an additional therapeutic agent, to include, for example, hydrocortisone or a glucocorticoid (p. 36, lines 1-16), as recited by claims 39 and 41.

However, Bendtzen does not teach derivatives of fusidic acid having a polyamine group corresponding to formulae VIII, X, XI, XII, XIII, XVI, XVII, XVIII, XIX, XXII, or XXIII at C_3 (R11) or C_{21} (R2), as recited by the instant claims.

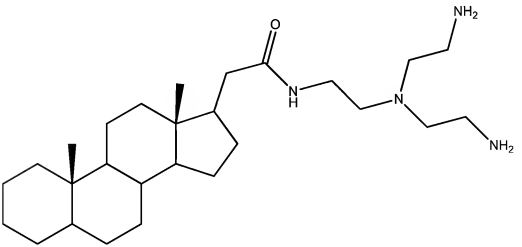
Mintz et al. disclose methods of treating infections or diseases caused by an infectious agent (abstract), particularly bacterial or fungal infections, by administering compounds of general formula (I) (col. 1, lines 5-8):



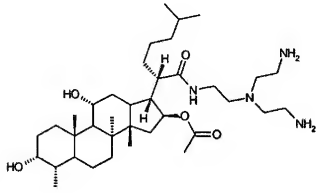
In particular, R_4 can be –C(O)-NHR$_6$, a polyamine group wherein R_6 has the structural formulae set forth in Figs. 1 and 2, in particular



Where R1, R2, and R3 are hydrogen, n = 0, R_4 is –C(O)-NHR$_6$, and R6 is the N-(2-(bis (2-aminoethyl)amino)ethyl moiety shown above, this yields a compound having the structural formula,



wherein the polyamine group at C_{21} corresponds to the 21-N-{2'-[bis (2'aminoethyl)amino]ethyl} polyamine group at C_{21} of elected compound 101,

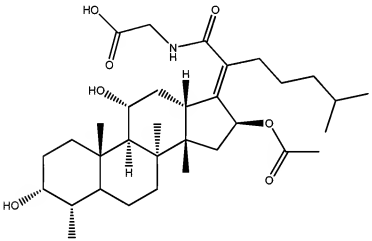


as recited by claim 26 (i.e., the first listed species on page 9 of the claims). In addition, the compounds of Mintz et al. possess antibiotic activity against a wide variety of microorganisms, to include gram-positive and gram-negative bacteria (col. 5, lines 59-67; col. 8, line 57 to col. 9, line 11) and may therefore be used to prevent or treat bacterial infections, as well as to serve as disinfectants for suppressing bacterial growth on surfaces such as surgical instruments (col. 2, lines 6-19).

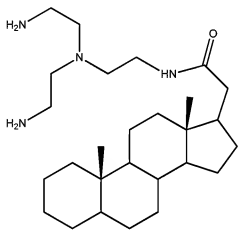
Thus, Mintz et al. further teach the disclosed compounds in pharmaceutical compositions (col. 6, line 43 to col. 8, line 31), as recited by claims 27 and 39, which can be administered in combination with an additional therapeutic agent, to include fusidic acid, and, for example, cephalosporins, penicillins, lincomycin, clindamycin, tetracyclines, and erythromycin (col. 8, lines 32-56), as recited by claims 39 and 41.

Mintz et al. differs from the claimed compounds in that the compounds of Mintz et al. are derived from cholane rather than fusidic acid.

However, the compounds of Bendtzen et al. are derived from fusidic acid and have a C_{21} secondary amine group; and a skilled artisan would have been motivated to substitute the C_{21} group of compound XVIa as taught by Bendtzen et al. with the C_{21} polyamine side chain taught by Mintz et al.,



Bendtzen et al.



Mintz et al.

because both the compounds of Bendtzen et al. and the compounds of Mintz et al. were disclosed to be useful in methods of treating bacterial infections by administration to a patient having such an infection. Because the compounds of both references were known for the same use, one of ordinary skill in the art would have had a reasonable expectation of success modifying C_{21} of compound XVIa as taught by Bendtzen et al. with the C_{21} polyamine side chain taught by Mintz et al. to arrive at the elected compound 101 having antibacterial activity, as recited by the instant claims.

CONCLUSION

Claims 1, 6, 7, 12, 14, 26, 27, 33, and 39-41 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612